

[illegible]

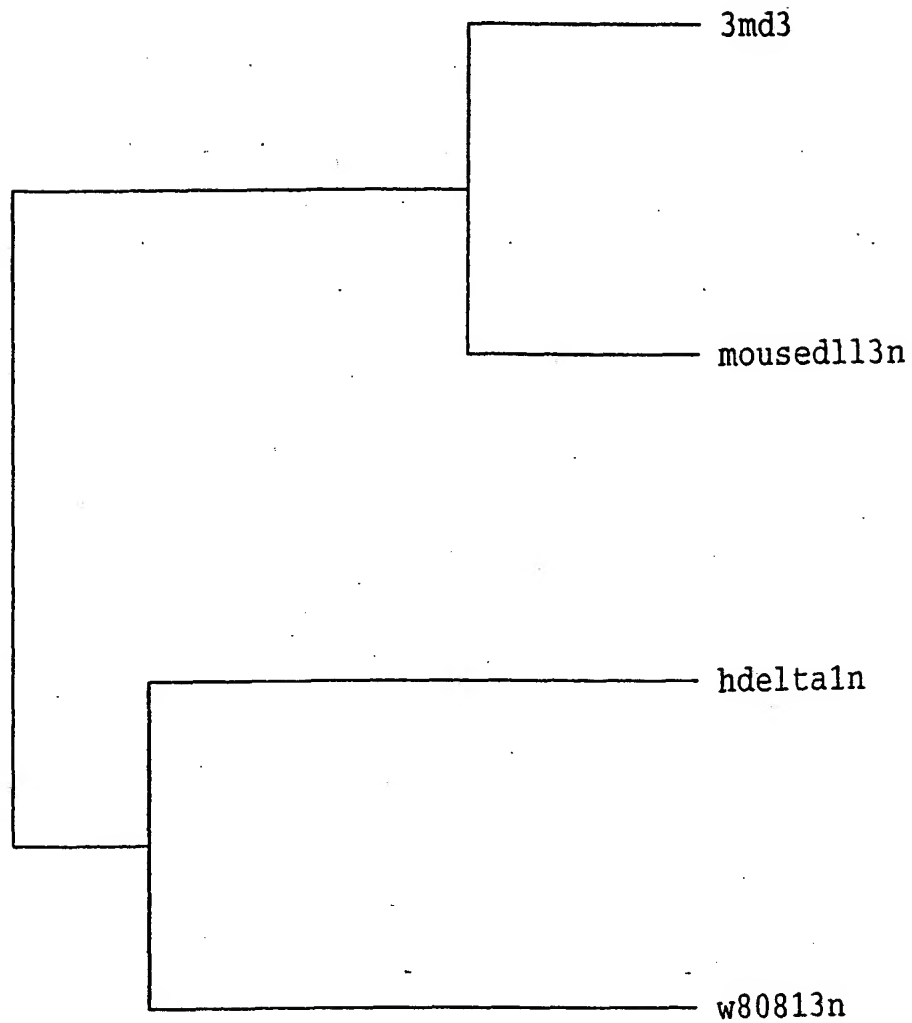


FIGURE 2

[illegible]

FIGURE 3B

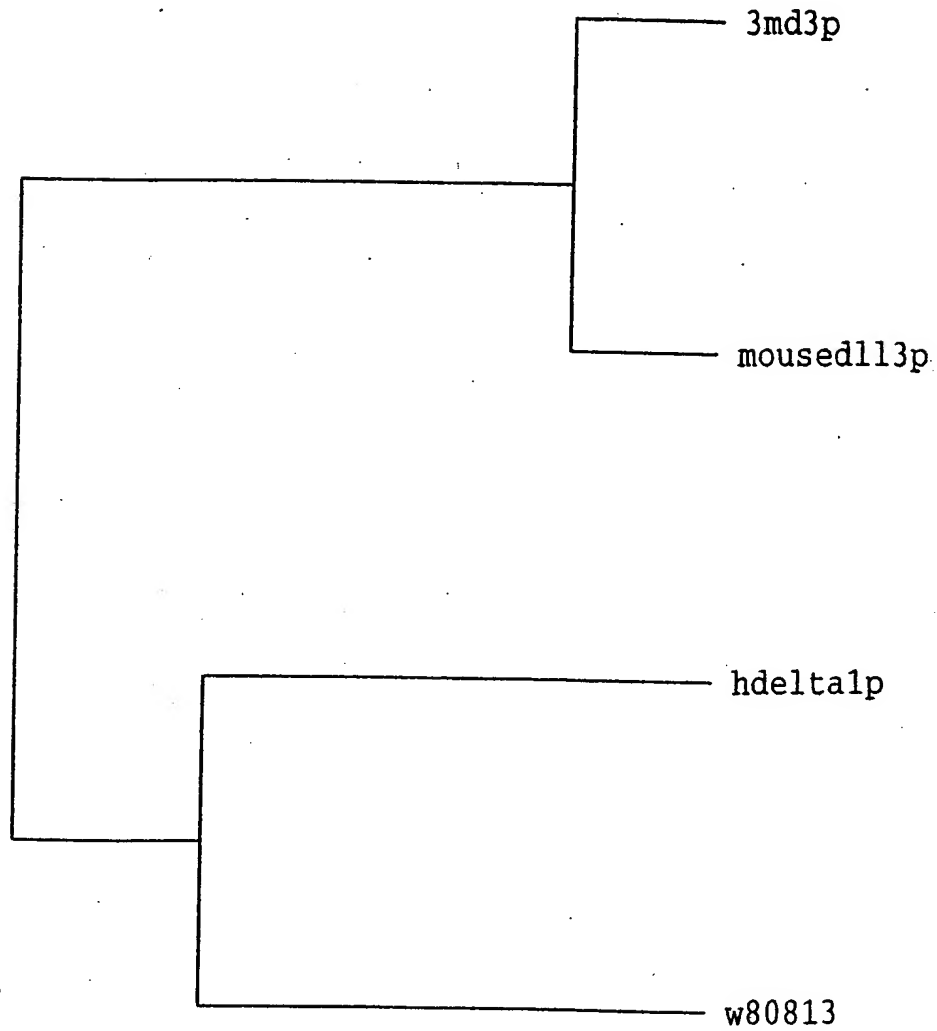


FIGURE 4

3md3 Nucleotide Sequence: 1752 (SEQ ID NO:1)

ATGGTCTCCCCACGGATGTCCGGGCTCCTCTCCCAGACTGTGATCCTAGC
GCTCATTTTCTCCCCCAGACACGGCCGCTGGCGTCTTCGAGCTGCAGA
TCCACTCTTTTCGGGCCGGGTCCAGGCCCTGGGGCCCCGCGGTCCCCCTGC
AGCGCCCGGCTCCCTGCGCCTCTTCTTCAGAGTCTGCCTGAAGCCTGG
GCTCTCAGAGGAGGCCGCGAGTCCCCGTGCGCCCTGGGCGCGGCGCTGA
GTGCGCGCGGACCGGTCTACACCGAGCAGCCGAGCGCCCGCGCCTGAT
CTCCCACTGCCCGACGGCCTCTTGACAGGTGCCCTTCCGGGACGCTGGCC
TGGCACCTTCTCTTTCATCATCGAAACCTGGAGAGAGGAGTTAGGAGACC
AGATTGGAGGGCCCGCTGGAGCCTGCTGGCGCGCTGGCTGGCAGGCGG
CGCTTGGCAGCCGGAGGCCCGTGGGCCCCGGACATTAGCGCGCAGGCGC
CTGGGAGCTGCGCTGCTCGTACCGCGCGCGCTGCGAGCCGCTGCGGTGC
GGACCGCGTGACCGCGCCTCTGCCGTCCGCGCAGCGCCCCCTCGCGGTGC
GGTCCGGGACTGCGCCCCCTGCGCACCGCTCGAGGACGAATCGGTGTGCGG
AGCAGGCTGCAGCCCTGAGCATGGCTTCTGTGAACAGCCCGGTGAATGCC
GATGCCTAGAGGGCTGGACTGGACCCCTCTGCACGGTCCCTGTCTCCACC
AGCAGCTGCCTCAGCCCCAGGGGCCGCTCTGTGCTACCACCGGATGCCT
TGTCCCTGGGCTGGGCCCTGTGACGGGAACCCGTGTGCCAATGGAGGCA
GCTGTAGTGAGACACCCAGGTCCTTTGAATGCACCTGCCCGCGTGGGTTT
TACGGGCTGCGGTGTGAGGTGAGCGGGTGACATGTGCAGATGGACCCTG
CTTCAACGGCGGCTTGTGTGTGCGGGGTGCAGACCCTGACTCTGCCTACA
TCTGCCACTGCCACCTGGTTTCCAAGGCTCCAAGTGTGAGAAGAGGGTG
GACCGGTGCAGCCTGCAGCCATGCCCAATGGCGGACTCTGCCTGGACCT
GGGCCACGCCCTGCGCTGCCGCTGCCGCGCGCGCTTCCGCGGTCTCTCGT
GCGAGCACGACCTGGACGACTGCGCGGGCCGCGCCTGCGCTAACGGCGGC
ACGTGTGTGGAGGGCGGCGCGCACCGCTGCTCCTGCGCGCTGGGCTT
CGGCGGCCGCGACTGCCGCGAGCGCGCGGACCCGTGCGCCGCGCGCCCT
GTGCTCACGGCGCGCGCTGCTACGCCCACTTCTCCGGCCTCGTCTGCGCT
TGCGCTCCCGGCTACATGGGAGCGCGGTGTGAGTTCCCAGTGCACCCGA
CGGCGCAAGCGCCTTGGCCGCGGCCCGCGGCGCTCAGGCCCGGGGACC
CTCAGCGCTACCTTTTGCTCCGGCTCTGGGACTGCTCGTGGCCGCGGGC
GTGGCCGGCGCTGCGCTCTTGCTGGTCCACGTGCGCGCCGCTGGCCACTC
CCAGGATGCTGGGTCTCGCTTGCTGGCTGGGACCCCGGAGCCGTCACTCC
ACGCACTCCCGGATGCACTCAACAACCTAAGGACGACGAGGAGGTTCCGGG
GATGGTCCGAGCTCGTCCGTAGATTGGAATCGCCCTGAAGATGTAGACCC
TCAAGGGATTATGTCATATCTGCTCCTTCCATCTACGCTCGGGAGGCCT
GA

FIGURE 5A

3md3 Protein Sequence: 583 (SEQ ID NO:2)

MVSPRMSGLLSQTIVILALIFLPQTRPAGVFELQIHSEFGPGPGPGAPRSPCS
ARLPCRLFFRVCLKPGLSEEAESPALGAALSARGPVYTEQPGAPADLP
LPDGLLQVPFRDAWPGTFSFIIETWREELGDQIGGPAWSLLARVAGRRRLA
AGGPWARDIQRAGAWELRCSYRARCEPPAVGTACTRLCRPRSAPSRCGPGL
RPCAPLEDESVCRAGCSPHGFCEQPGECRCLEGWTGPLCTVPVSTSSCLS
PRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRCE
VSGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFGSNCEKRVDRCSLQP
CRNGGLCLDLGHALRCRCRAGFAGPRCEHDLDDCAGRACANGGTCVEGGGA
HRCSCALGFGGDRDCRERADPCAARPCAHHGGRCYAHFSGLVCAAPGYMGAR
CEFPVHPDGASALPAAPPGLRPGDPQRYLLPPALGLLVAAGVAGAALLLVH
VRRRGHSQDAGSRLLAGTPEPSVHALPDALNNLRTQEGSGDGPSSSSVDWNR
PEDVDPQGIYVISAPSIYAREA

FIGURE 5B

FIGURE 6

2hd1 nucleotide sequence (SEQ ID NO:3)

AGTACTCCTACCGCTTCGTGTGTGACGAACACTACTACGGAGAGGGCTGCTCCGTTTTCT
GCCGTCCCCGGGACGATGCCTTCGGCCACTTCACCTGTGGGGAGCGTGGGGAGAAAGTGT
GCAACCCCTGGCTGGAAGGGCCCTACTGCACAGAGCGTGAGTCTCTGGGAAGGCACCGCT
GGCTCACTCGTCCACGAACACGGACCACGCGCAGGGACGGGGCTTCTGAGCCACGGGGG
GCTTGGGACTGTAGAGATGTTCTGGTGGGGAACTGAGGCCAGAGGACAGAAGTGGATT
GCTATAAGTACAGCTCGTCAGTGGGGGGGTGGGGTCAACGCAGACATTTAAACATCCC
AGGCTGTGTTTATCCACTATCGGAAGTGCCTTTCTTAATCAGGGAGGATTTAGAGACAG
GGCCAGGGGTCAGGAAGTAAAGCCAGTGCTACCCCCARGGTGTGTATTAGAGAGGGAG
AGGAGGAAGGAAGGGAGGAACACAGAGAGAGCTTGTGTGTGAGGGGCACCATTTCACCC
GAGTTCCAGTGCTGGAACAGCATCACACTGGGAAACGTTCCATTTCTCTCTGGAGCTG
GTGTGCTTGACCTCTCTGGAGCAAACGCCTTTCGGATACTCCCTGTGACACGCACTGTC
TATGCTGGCCAGAGAGCAGGCTTTCACTCCTGTGGGCTGCTGAGGCCAGGTCTCCAAGGC
CTGTGTGGGCGAGGGGTGCACAGCCCGTCTGGCTTGAATGCTCAGGCAGCACCTTGTCT
GGAAAAGCAATGTCTTCCCAATAGTGACAGAGGCTCTACCTGCCTCTTATTAGGTATTGA
TGTGTCAATGTCTATGGCAGGCAGGTGACTAGGGCAGGGTTGGGGCCGTGCTGGCTCCTGG
TTCTGGCTCATGGGGACCTCAGGAGCCCTCTCTCCAGCTGACTGAGGCCTCGCCTGCAGC
CCTGGCCCGTCCCAGCCCATTTGGTACCGGATTTCTCTACAGCTGGGGATTGGGTAGGTCC
TGGAGCTGCCCGAGAACTCCAGGGAAGTGTCACTTCTCCTTGGAACTGGACAACCTT
GGAGAGGGGCTCTGGGAGGCCAGAACCTCTGGCAGGAGCTGGGTAGTGCCTGGGGTTGA
GGGTGGGTCTTCCCATTCCTGAGTGCCTTGATGTCTTGTCTCCTTAGCTTCCCAAATTC
CCTCCGGAAGTACTGAGCTCCTTCTAAGCTTTCCTTGGCCTGAACTGGTTCTGGGGAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

2hd1 protein sequence (SEQ ID NO:4)

GRIDLKYSYRFVCDHYHGGCSVFPCRPRDDAFGHFTCGERGEKVCNPGWKGPYCTERES
LGRHRWLTRPRTTRRDGAS

FIGURE 7

Notch signaling

Upon binding to Delta or Jagged (Notch ligands), the intracellular domain of Notch is cleaved by a presenilin-dependent pathway and translocates to the nucleus along with DNA-binding protein, CSL, to activate transcription of downstream genes. The intracellular domain of Notch also downregulates the JNK pathway through a CSL independent mechanism. Modulators of the pathway includes Kuzbanian, an ADAM protease that positively regulate Notch signaling, and Fringe, a putative glycosyltransferase that inhibits Jagged signaling.

